Citation:

Oken E, Wright RO, Kleinman KP, Bellinger D, Amarasiriwardena CJ, Hu H, Rich-Edwards JW, Gillman MW. Maternal fish consumption, hair mercury, and infant cognition in a U.S. Cohort. *Environ Health Perspect.* 2005 Oct;113(10):1376-80.

PubMed ID: 16203250

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To examine the associations of maternal fish and seafood intake and maternal hair mercury at delivery with 6-month infant cognition in a U.S. cohort.

Inclusion Criteria:

- Women who presented at their initial clinical visit at < 22 weeks of gestation
- Had a singleton pregnancy
- Were able to complete study forms in English
- Did not plan to move out of the study area before delivery.

Exclusion Criteria:

None noted by author.

Description of Study Protocol:

Recruitment Study subjects were participants in Project Viva, a prospective cohort study of gestational diet and other exposures, pregnancy outcomes, and offspring health in eastern Massachusetts. Women were recruited at their initial clinical obstetric appointment.

Design: Prospective Cohort study

- At the initial visit demographic characteristics, health history, and health habits were collected by interview and a self-administered questionnaire. Infant birth weight and gestation length were obtained from medical records.
- At the second study visit, performed at 26-28 weeks of gestation, participants completed a semiquantitative food frequency questionnaire, which had been previously calibrated against blood levels of long-chain marine n-3 fatty acids. Second semester fish exposure was used, as the timing of intake assessed by the questionnaire best overlapped with the timing of mercury exposure assessed by the maternal hair length studied. Maternal hair samples were collected during the hospitalization

for the delivery. 50-100 strands of hair were collected. In addition, participants were asked about potential mercury occupational exposure. The hair samples were analyzed for mercury through mercury assay using the Direct Mercury Analyzer 80.
- Infants underwent cognitive testing at approximately 6 months of age using visual recognition memory (VRM) paradigm. Trained test administrators presented the infants with two identical photographs of an infant's face, at a standardized distance. The habituation trials were repeated with no maximum number of presentations until the infant began habituated to this stimulus. In the testing stage, the infant was presented with the previously seen photo simultaneously with a novel photo of another infant's face. The test administrators tracked the amount of time that the infant looked at each stimulus and then calculated a novelty preference (percentage of the total test time that the infant spent looking at the novel stimulus). The test administrator recorded his/her confidence that the test was performed without distractions.
- Each infant had two test trials and the final score represents the average of the two trials.

Blinding used (if applicable): not applicable.

Intervention (if applicable): not applicable

Statistical Analysis

- Linear regression was used to assess factors associated with VRM score. Individual bivariate analyses with each maternal and child characteristic was performed first. For multivariable analyses, both maternal hair mercury obtained at delivery and maternal second-trimester weekly intake of combined seafood and fish as well as the covariates maternal age, race/ethnicity. education, and marital status and infant sex, gestational age at birth, birth weight for gestational age, breast feeding duration and age at cognitive testing were included as independent predictors of VRM score.
- Both mercury levels and fish intake were studied as continuous predictors. Fish intake and mercury exposure based on public health recommendations were also dichotomized.
- All final models met standard assumptions for linear regression.

Data Collection Summary:

Timing of Measurements

- At the initial visit demographic characteristics, health history, and health habits were collected by interview and a self-administered questionnaire. Infant birth weight and gestation length were obtained from medical records.
- At the second study visit, performed at 26-28 weeks of gestation, participants completed a semiquantitative food frequency questionnaire. Maternal hair samples were collected during the hospitalization for the delivery.
- Infants underwent cognitive testing as approximately 6 months of age.

Dependent Variables

- Offspring cognitive scores (VRM)

Independent Variables

- Fish intake - measured by weekly number of serving either as > 2 servings/week or </= two servings per week and as a continuous variable
- Hair mercury level at time of delivery > 1.2 ppm or </= 1.2 ppm and as a continuous variable

Control Variables

- Maternal age
- Race/ethnicity

- Education
- Marital status
- Infant sex
- Gestational age of infant
- Birth weight of gestational age
- Breast feeding duration
- Age at cognitive testing

Description of Actual Data Sample:

Initial N: 2,128 participants delivered a live infant. During the sampling period 409 participants delivered, 302 were approached for collection of a hair sample. 211 consented to the hair sample.

Attrition (final N): 135 mother-infant pairs

Age:16% were < 30 years, 53% were 30-34 years, 31% were >/= 35 years.

Ethnicity:White 82%, Nonwhite 18%

Other relevant demographics:

- College education or greater: 80%, < college graduate 20%.
- 94% breast-fed their infant and 50% continued to breast-feed until at least 6 months postpartum.
- 79% consumed some alcohol, although only 19% continued to consume alcohol after learning they were pregnant, 7% reported smoking.
- Use of these substances were not related to maternal hair mercury or to fish consumption.
- Six infants were born preterm.

Anthropometrics

Location:Eastern Massachusetts

Summary of Results:

Key Findings

- Mothers consumed an average of 1.2 fish servings per week during the second trimester
- Mean maternal hair mercury was 0.5 ppm, with 10% of samples > 1.2 ppm.
- Mean VRM score was 59.8 (range 10.9 - 92.5).
- Higher mercury exposure in pregnancy is associated with lower offspring cognitive scores, even at low levels of exposure.
- Higher maternal fish intake was associated with higher mercury levels.
- Higher fish consumption was associated wish better infant cognition. This benefit was greater among infants whose mothers consumed more fish but had lower mercury levels.
- For each additional weekly fish serving, offspring VRM score was 4.0 points higher (95% confidence interval: 1.3 to 6.7).
- An increase of 1 ppm in mercury was associated with a decrement in VRM score of 7.5 (95% confidence interval: -13.7 to -1.2) points.
- VRM scores were highest among infants of women who consumed >2 weekly fish servings but had mercury levels <1.2 ppm.

Associations of maternal second-trimester fish consumption and maternal hair mercury at delivery with infant cognition at 6 months (VRM score): results from six linear regression models among 135 mother-infant pairs in Project Viva.

Model	Change in VRM score [%novelty preference (95% CI)] Effect per weekly fish serving	Change in VRM score [%novelty preference (95% CI)] Effect per ppm maternal hair mercury
Fish only	2.5(-0.01 to 5.0	___
Fish and participant characteristics	2.8(0.2 to 5.4)	___
Mercury only	___	-4.6(-10.3 to 1.1)
Mercury and participant characteristics	___	-4.0(-10.0 to 2.0)
Fish and mercury	3.9 (1.2 to 6.5)	-8.1(-14.1 to -2.0)
Fish, mercury, and participant characteristics	4.0 (1.3 to 6.7)	-7.5 (-13.7 to -1.2)

*Participant characteristics adjusted for age, race/ethnicity, education, marital status, infant sex, gestational age at birth, birth weight, breast-feeding duration and age at cognitive testing.

Mean cognitive (VRM) scores (% novelty preference) among offspring of mothers with high or low second-trimester fish intake and high or low hair mercury levels at delivery.

Weekly fish intake	Hair mercury </= 1.2 ppm	Hair mercury > 1.2 ppm
> 2 servings	72 (n=7)	55(n=2)
</= 2 servings	60(n=114)	53 (n=12)

Author Conclusion:

- Higher mercury exposure in pregnancy is associated with lower offspring cognitive scores, even at low levels of exposure.
- Higher maternal fish intake was associated with higher mercury levels, however higher maternal fish consumption was associated with better infant cognition.
- This benefit appeared greatest among infants whose mothers consumed more fish but had lower mercury levels.

Reviewer Comments:

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A

3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A

7.	**Were outcomes clearly defined and the measurements valid and reliable?**		Yes
	7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
	7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
	7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
	7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
	7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
	7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
	7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**		Yes
	8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
	8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
	8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
	8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
	8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
	8.6.	Was clinical significance as well as statistical significance reported?	Yes
	8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**		Yes
	9.1.	Is there a discussion of findings?	Yes
	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**		Yes
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	Yes